



Appendix 2. Informed Consent Letter

“Efficacy and safety of zinc sulfate to reduce the duration of acute diarrheic disease between 6 and 59 months of age”

Please take all the time needed to read this document. In case you cannot read it, request for it to be read in detail. In case the person responsible for the minor does not speak Spanish, look for a reliable translator or interpreter.

Introduction

The acute diarrheic disease in children under 5 years of age is the cause of 20% of health services consultations, this is, 20 out of every 100 children that are taken to a consultation have diarrhea. In Mexico this disease occupies the fifth place amongst the causes of death in this age group. Therefore efforts are being made for the treatment of diarrhea to include everything proven to be useful. Some studies have proven that giving zinc during diarrhea decreases not only the intensity and duration of diarrhea, but also decreases the probability that the child presents diarrhea again in the following months. Zinc supplements are often used in our population and there are some programs of infant attention that already includes them between the supplements given to underage children.

Study objective

This investigation pretends to evaluate the effect of zinc (a mineral micronutrient) over the duration, severity and relapse of acute diarrheic disease, in children between 6 and 59 months of age, like yours. Qualified physicians will manage the identification of the minors with acute diarrhea.

The participating Medical Units are public and count with the services, personnel and resources necessary for the attention of children with acute diarrhea, in which it is expected to include at least 516 children from 6 to 59 months of age with this diagnose.

The present study is under the direction, supervision and funding of the National Public Health Institute and the United Nations Children's Fund (UNICEF). This study counts with the approval of the corresponding Ethics Committees and the participant Medical units.

Study procedure

We are inviting you to have your child participate in this study because he/she has acute diarrhea. If you choose that your child participate in the study, we will ask specific elaborate questions for the investigation. In the first part we will ask personal contact and location information that will be useful to contact you afterwards for the collection of information about your child's health state. In the second part, we will ask questions about some general characteristics of your child's surroundings, important health backgrounds, immunization records and about the current diarrheic episode. In case it's necessary, additional information from the clinical record will be obtained. There will be measuring and weigh in of your child. The duration of time to ask the questions will be of 15 to 20 minutes.

Two five milliliters blood samples will be taken (equivalent or similar to a teaspoon) during the study to measure Hemoglobin, albumin, and zinc levels. The first sample will be taken at the beginning of the study and the second one within the first 4 months after the initial, the physician responsible of the study will notify you when your child is due for the second sampling within this period. Trained personnel will take the sample, from the vein of one of your child's arms.



There will also be a collection of stool from your child's diaper in the next 24 hours to their medical attention in this Unit. The stool samples will be utilized only to detect the presence of microorganisms causative of diarrhea.

Samples will be processed and analyzed in the National Public Health Institute only for the means commented previously.

Children will receive the treatment that in the physician's judgment is the more adequate for their disease, age and clinical state. Moreover, as part of the study, through a draw (like flipping a coin) your child will be assigned to one of two of the study groups, this is, will have the same probability to get any of the following groups:

- One study group will receive a tablet, which needs to be diluted in water and given to your child once a day for 10 days; this tablet contains 20 mg of zinc.
- The other study group will receive a tablet, which will have to be diluted in water and given to your child once a day for 10 days; the only difference is that this tablet does not contain zinc, it is a tablet that we will use as control like placebo.

Neither your doctor nor yourself will know in what treatment group your child is. The responsible physician of the study in this center will hand the tablets, once you accept to participate.

During the diarrhea picture in your child we will call every day until the total restore of your child. Afterwards, once a week we will call you over the phone to ask if your child has presented new diarrheic pictures that week. It is very important to clarify that if your child presents diarrhea you should go to consultation as done regularly every time your child gets sick with anything. This is, you should not wait to receive a phone call. In total it will be one phone call a week for a year.

Risks and inconveniences related to the study

Whether your child participates in this study does not imply a health risk, since the fact of receiving a placebo is acceptable because zinc supplement is not a part of the usual handling of diarrhea in Mexico, and in case of getting zinc that does not represent any risk either because of the dosage that is going to be administered, which is already recommended and has proven to be safe in other countries. The consequences of consuming zinc are rare, but could be abdominal pain, dyspepsia, nausea, vomit, diarrhea, gastric irritation and gastritis. The amount of blood that is going to be taken from your child is small, and will be only in two occasions in a year, the discomfort could be pain at the moment of puncture or a small bruise that will disappear in a few days. The stool sample will be collected directly from the diaper, so your child will not be submitted to invasive diagnostic procedures.

The treatment or any attention given will be standard and usual, so they will not have any damage related to the investigation.

Potential benefits of the study

It is probable that your child does not receive a direct benefit for participating in the study, nevertheless, the results of the study will allow to establish if the administration of zinc is useful in acute diarrheic disease in Mexican children under the age of 5 years of age and this will be a benefit for society as a whole because if it is useful it could be incorporated to the usual diarrhea treatment. In case it is proven that zinc is of utility, and your child has received the tablet not containing zinc, this is the placebo, we will commit to giving zinc for 10 days in case of presenting a new diarrheic picture after the end of the study.



Confidentiality and privacy notice.

All the information collected from your child for this study will be considered confidential according to the law. To protect your and your child's privacy, the records will be handled using numeric codes; your names will only be registered in this Informed Consent Letter, in the Case Report Form and Follow-up Form. Data registered will be handled as confidential; they will be kept in secure files inside of the Medical Units and of the study's central coordination. Your child's data will only be able to be reviewed by people that work in the study and are detailed at the end of this letter. The name of the parents or guardians of the minor, or other data that could identify you will not appear in any report, nor in informs related to this study. Your and your child's information collected in this study, as well as the stool and blood samples, will only be used for the same ends.

Cost: There is neither cost nor payment for you if your child participates in the study.

Voluntary participation and withdrawal from the study

You can freely and voluntarily choose whether your child is a part of this study or not. You can stop answering the questions at any time and for any reason. You can also decide to withdraw your child from the study at any time. If you decide that your child does not participate, or if you leave the study, your child will not lose any health care services. If you decide to have your child participate, we request that the information you give us about your child's health, health history and contact information be truthful, and allow us to telephone you to collect information daily during the days that your child has diarrhea, and weekly for the duration of the study or visit your home if necessary

Normative basis

This informed consent complies with the guidelines established in the General Health Law, in the Regulations of the General Health Law in Health Research Matter, in the Helsinki Declaration of the World Medical Association for Ethics Principles for Human Medical Research, and in the International Ethics Guidelines for Biomedical Research in Humans of the Counsel for the Medical Sciences International Organization in collaboration with the World Health Organization. The Research Ethics Committees in the health units in which the investigation is performed are the ones responsible of looking over these rights, so if being necessary you may contact the Ethics Committee of the National Health Institute, to the telephone number 01 777329 3000 extension 7424 Monday to Friday from 8:30 to 16:30 hours or if you rather write to the following email address: etica@correo.insp.mx. If you have any questions or want to speak to someone regarding this study you may contact Dr. Edgar Sánchez Uribe, study coordinator, to the cellphone 044 55 5452 7856.

**Kinship or relation**

**Name and signature of witness 1**

Name(s) *Last name 1* *Last name 2* *Signature* *dd / M M M / y y y y*
Date

Address witness 1

Telephone: _____ **Relation or kinship with the minor**
: _____

Name and signature of witness 2

Names(s) *Last name 1* *Last name 2* *Signature* *dd / M M M / y y y y*
Date

Address witness 2

Telephone: _____ **Relation or kinship with the minor:** _____

In case of analphabetism or the mother, father or guardian not being able to sign. A witness that knows how to read and write must sign. If possible the participants must select them and must not have any connection to the research team. The parents or guardians must include their fingerprint. I have been witness to the exact reading of this consent document to the potential participant; the individual has had the opportunity to ask questions. I confirm that the individual has given their consent to participate in this study freely and well informed.

<p>_____ Name and signature</p>	<p>_____ Date</p>	<p>Fingerprint (Mother or Father or Guardian)</p>
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This part must be complete by the researcher (or their representative):

I have explained to Mr. or Mrs. _____ the purposes of the investigation; I have explained the risks and benefits that their child's participation in the study implies. I have answered their questions and have asked if they have any doubts. Once concluded the questions and answers session, the present document proceeded to be signed.

Name and signature of the researcher that administers the consent *dd / M M M / y y y y*
Date

c. c. p. Patient or family member
c. c. p. Researcher (to be kept in the investigation's file)